due: 10/19/04

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JUL. 26. 2004
S. YAMAMOTO

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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JAPON

PCT

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)*	19.07.2004
Applicant's or agent's file reference CD005PCT	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP 03/15641	05.12.2003	05.12.2002

International Patent Classification (IPC) or both national classification and IPC
A61L27/50, A61L27/58, A61F2/06, A61F2/24

Applicant
CARDIO INCORPORATED et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 05.04.2005

Name and mailing address of the international preliminary examining authority:

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I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-192 as originally filed

Claims, Numbers

1-102 as originally filed

Drawings, Sheets

1/64-64/64 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   ☐ the language of publication of the international application (under Rule 48.3(b)).
   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:
   ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-102 (partially)

   because:

   ☒ the said international application, or the said claims Nos. 40-50,96-100 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☒ the claims, or said claims Nos. 1-102 are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 1-102

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the Standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-102
Inventive step (IS)	Claims	1-102
Industrial applicability (IA)	Claims	

2. Citations and explanations

   see separate sheet

Reference is made to the following documents:

D1: US 2002/165601 A1 (CLERC CLAUDE O) 7 November 2002 (2002-11-07)
D2: US-A-5 584 875 (DUHAMEL RAYMOND C ET AL) 17 December 1996 (1996-12-17)
D3: GB-A-2 280 372 (JOHNSON & JOHNSON MEDICAL) 1 February 1995 (1995-02-01)
D4: EP-A-0 636 378 (JOHNSON & JOHNSON MEDICAL) 1 February 1995 (1995-02-01)
D5: EP-A-0 194 192 (ETHNOR) 10 September 1986 (1986-09-10)
D6: US-A-5 741 257 (KIRSCH AXEL) 21 April 1998 (1998-04-21)
D7: US-A-5 948 020 (LEE SEUNG-JIN ET AL) 7 September 1999 (1999-09-07)
D8: WO 01/32229 A (SMITH & NEPHEW ; COTTON NICHOLAS JOHN (GB)) 10 May 2001 (2001-05-10)
D9: US-B-6 319 2641 (PAASIMAA SENJA ET AL) 20 November 2001 (2001-11-20)
D10: HEINO A ET AL: "Application of a self-reinforced polyglycolic acid (SR-PGA) membrane to the closure of an abdominal fascial defect in rats." JOURNAL OF BIOMEDICAL MATERIALS RESEARCH. 1999, vol. 48, no. 5, 1999, pages 596-601, XP002280760 ISSN: 0021-9304
D11: EP-A-0 943 298 (COUSIN BIOTECH S A S) 22 September 1999 (1999-09-22)
D12: WO 93/17635 A (BARD INC C R) 16 September 1993 (1993-09-16)
D13: WO 95/25482 A (ORGANOGENESIS INC) 28 September 1995 (1995-09-28)
D14: EP-A-1 023 879 (MEDTRONIC INC) 2 August 2000 (2000-08-02)

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 40-50,96-100 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article

34(4)(a)(I) PCT).

Those claims that are directed to in vivo implanting and organ regeneration should be strictly limited to non-humans and for non-therapeutical purposes.

The search was restricted under articles 5 and 6 PCT to the following :

An implant comprising:
- a first knit layer made of a biodegradable polymer
- a second woven layer made of a biodegradable polymer
Optional features:
- an intermediate biodegradable polymer layer
- a biomolecule attached to the first layer
- and all other technical features that appear in the claims and that are both founded by the description and clear

Further, a process for preparing the implant and a method of culturing the implant inside an non human organism for non therapeutical purposes.

NB: This is NOT a suggestion for an allowable claim. The applicant's charge is to propose claims that are clear and founded on the description, and that enable the skilled person to realise the invention (Art. 5 and 6 PCT).

Claims or parts of claims relating to inventions for which no Internaitional Search Report has been established cannot be subject of the International Preliminary Examination (Rule 66.1(e) PCT).

As none of the claims covers the searched invention, which is supported by the description and particularly by the examples, examination can only carried out on the searched invention and cannot refer to any claim.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 INVENTION

An implant comprising:

- a first knit layer made of a biodegradable polymer
- a second woven layer made of a biodegradable polymer

Optional features:

- an intermediate biodegradable polymer layer
- a biomolecule attached to the first layer
- and all other technical features that appear in the claims and that are both founded by the description and clear

Further, a process for preparing the implant and a method of culturing the implant inside an non human organism for non therapeutical purposes.

NB: This is NOT a suggestion for an allowable claim. The applicant's charge is to propose claims that are clear and founded on the description, and that enable the skilled person to realise the invention (Art. 5 and 6 PCT).

V.2 CLARITY

The objections made under Art. 5 and 6 in the International Search Report are maintained.

The applicant should delete all occurences of the relative term 'about', where this term refers to a range or to range limits.
Further the applicant should delete all statements similar to 'incorporated herein by reference'.

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description, nor is this document identified therein.

V.3 PRIOR ART

If not otherwise specified, subject matter of cited documents relates to the passages indicated in the search report.

D1 - US2002165601
A bioabsorbable stent graft made of a woven, knitted or braided inner (luminal) first layer made of biodegradable polymers (lactide, glycolide, etc.) and a second outer layer that is tighter woven, knitted or braided, made of biodegradable elastomers.

In an alternative, the second layer is made from the same biodegradable material as the first layer, and is woven.
The two layers are secured to each other through adhesive polymer solutions, of which the solvent is evaporated under heat.
No grafting of biomolecules is disclosed.

D2 - US5584875
A vascular graft made of a knitted biostable polymer that is soaked in a albumin or collagen solution (or virtually any biocompatible, bioerodible polymer such as polysaccharides and glycosaminoglycans) that is subsequently crosslinked.
The surface promotes cell ingrowth.

D3 - GB2280372
A composite layered implant comprising a collagen matrix poured onto a woven or knitted fabric made of a biodegradable polymer (such as a copolymer of lactic acid and glycolic acid: VICRYL), where the collagen matrix comprises oil droplets and can comprise a medicament (eg cytokine, growth factor, etc.) and can be optionnaly crosslinked.
The implant is to be used as a vascular prosthesis.

Cites EP0194192.

D4 - EP0636378
A composite layered implant comprising a collagen matrix poured onto a woven or knitted fabric made of a biodegradable polymer (such as a copolymer of lactic acid and glycolic acid), where the collagen matrix comprises a medicament, can comprise oil droplets and can be optionnaly crosslinked.
The implant is to be used for periodontal disease.

Cites EP0194192.

D5 - EP0194192
A composite layered implant comprising a collagen matrix poured onto a knitted fabric made of a biodegradable polymer (such as a copolymer of lactic acid (10%) and glycolic acid (90%) = VICRYL).
Alternatively, the implant can be made of two identical (knitted) fabrics.
The implant is to be used as a vascular prosthesis.

Cited in EP0636378.

D6 - US5741257
A layered bone membrane for healing a recess comprising a plurality of woven or knitted layers of different textures made from biodegradable material such as collagen, polylactide/VICRYL, polylactide.
The specific embodiments describe a membrane made of four woven collagen layers.

D7 - US5948020
An implantable resorbale membrane made of a woven or knitted fabric layer of biodegradable polymers (lactide, glycolide, etc.) and a coating made by applying a coating solution comprising a biodegradable polymer (lactide, glycolide, caprolactone, etc.) and a pore forming agent to the fabric layer.

D8 - WO0132229
A connective tissue implant comprising two layers made by different yarn treating methods, wound into a spiral.
The examples disclose a felt attached to a braided/knitted layer.
The fibers are made of bioabsorbable polymers (PGA,PLA, etc).

D9 - US6319264
A hernia mesh comprising a first layer made of DEXON MESH (knitted PGA fibres, see NLM10490672) and a second layer made of poly(L/D lactide), knitted. The two layers were sown together.
A third optional film layer made of bioabsorbable polymers is positioned on top.

D10 - XP002280760 - NLM10490672
Hernia membrane made of DEXON-MESH (knitted PGA fibres) and a strip of muscle tissue.

D11 - EP0943298
A surgical plate made from a woven or knitted textile made of a non resorbable polymer or a mixture of resorbable and non-resorbable material, an adhesive layer (thermosetting or thermo-curable) and a composite glass-PTFE porous sheet.

Cites WO9317635.

D12 - WO9317635

A prosthesis for limiting postoperative adhesions, comprising a first knitted layer made of biostable or biodegradable (VICRYL) polymers, attached through a silicone adhesive to a barrier layer made of a silicone elastomer sheet or a PTFE mesh.

Cited by EP0943298.

D13 - WO9525482
Implants made of three-dimensional bioabsorbable woven or knitted collagen fibres.

D14 - EP1023879
Prosthetic heart valves made of biostable polymers consisting of a body portion or an underlayer covered by an outer layer of woven or knitted biostable polymer or collagen fibers, where this outer layer is porous and rough to permit cell ingrowth.
Therapeutic agents, mainly to prevent an inflammatory response to the implant, can be included in the body part.
For the body part, a collagen sponge is also envisaged.
Medical devices made from polymers are known to contain therapeutic agents.

V.4 NOVELTY
Remarks under Art. 33(2) PCT

Document D1 anticipates the invention where it has either no optional features or where it has an intermediate biodegradable polymer layer.

The invention appears to lack novelty partially.

V.5 INVENTIVE STEP
Remarks under Art. 33(3) PCT

It appears obvious to provide a collagen coating on the luminal side of a vascular graft such as a stent of which patency is of mayor interest, given that it is in close contact with blood stream. The skilled person was aware of using collagen to solve this problem, as it is an established solution at least since 1996, the year in which D2 was disclosed and the latter describing the use of collagen for such a purpose.

The invention appears to lack inventive step.